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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/843,037	04/26/2001	Charles M. Buchanan	05015.0366U3	7210

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ATLANTA, GA 30303-1811

EXAMINER

MAIER, LEIGH C

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/843,037

Applicant(s)

Buchanan

Examiner

Leigh Maier

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on election filed April 23, 2003
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-90 is/are pending in the application.
- 4a) Of the above, claim(s) 1-15, 24-83, and 87 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 88 is/are allowed.
- 6) ☒ Claim(s) 16-23, 84-86, 89, and 90 is/are rejected.
- 7) ☐ Claim(s) is/are objected to.
- 8) ☐ Claims are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. application from the International Bureau (PCT Rule 17.2(a)).
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4, 5, 1C
- 4) ☐ Interview Summary (PTO-413) Paper No(s)
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

Election/Restriction

Applicant's election with traverse of Group II, claims 16-23 and 84-90 in Paper No. 9 is acknowledged. The traversal is on the ground(s) that the examiner has not shown that the search and examination of the entire application cannot be made without serious burden. This is not found persuasive because as set forth in the restriction requirement, the claims are drawn to different inventions requiring the search of several different classes and subclasses. In addition to the search of the required classes and subclasses, a comprehensive search of the prior art also requires a search of databases of foreign patents and non-patent literature, making a search of all the varied inventions to be burdensome.

Upon election of Group II, a further election of species was required. Applicant has elected pharmaceutically active guest molecules. All of the claims in Group II, except for claim 87, drawn to an inclusion complex comprising a fragrance, read on this species. Therefore, claim 87, along with the claims of Groups I, III, and IV – claims 1-15 and 24-83 – have been withdrawn from consideration.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite “. . . wherein the acylated cyclodextrin host molecule is about [80 or 90] % (wt.) to about 100% (wt.) substituted.” It is not clear how Applicant contemplates calculating weight % substitution. It is further unclear how a cyclodextrin could have 100 *weight* % substitution. The specification discusses cyclodextrin substitution at page 9, lines 9-14, wherein the percent substitution refers to percentage of available hydroxy groups are substituted. However, this has nothing to do with a *weight* percentage, so the claims are rendered vague and indefinite.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 16-18, 20-23, and 85 are rejected under 35 U.S.C. 102(b) as being anticipated by UEKAMA et al (US 5,904,929).

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UEKAMA discloses an inclusion complex comprising isosorbide dinitrate (mw = 236) and trivaleryl- β -cyclodextrin (mw = 2408). This inclusion complex comprises about 9 wt% of the guest molecule.

Claims 16-23 and 84 are rejected under 35 U.S.C. 102(b) as being anticipated by NAKANISHI et al (Biol. Pharm. Bull., 1997).

NAKANISHI discloses the preparation of a complex of the poorly soluble compound, flufenamic acid (mw = 275), and triacetyl- β -cyclodextrin (mw = 2016). See all of page 66. A complex of these components comprises 12 wt% of flufenamic acid.

Claims 16-23 and 85 are rejected under 35 U.S.C. 102(b) as being anticipated by SOLIMAN et al (Pharm. Sci., 1996).

SOLIMAN discloses the preparation of a complex of the water soluble compound, diltiazem (mw = 414), with triacetyl- β -cyclodextrin (mw = 2016) and with peroctanoyl- β -cyclodextrin (mw = 4074). See all of page 533. The wt% of the diltiazem in these inclusion complexes is 17% (about 15%) and 9%, respectively.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 16-18 and 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over HIRAYAMA et al (Kobunshi Ronbunshi, 1982) and UEKAMA et al (US 5,904,929). Because the HIRAYAMA reference is in the Japanese language, the examiner is relying in part on the Caplus abstract of the journal article.

The invention is drawn to inclusion complexes comprising an acylated cyclodextrin and a guest molecule wherein the guest molecule comprises from about 2 wt% to about 15 wt% of the inclusion complex. (Applicant has elected "pharmaceutical actives" as guest molecules.)

Dependents further limit the wt% of guest molecule; type of acyl group; and type of cyclodextrin.

HIRAYAMA teaches inclusion complexes of a Δ -prostaglandin methyl ester (ONO-802; mw = 376) with α -, β -, and γ -cyclodextrin for the preparation of a controlled release product.

See abstract. The reference does not teach the use of acylated cyclodextrins.

UEKAMA teaches the use of per-C₂₋₁₈ acylated (α -, β -, and γ -)cyclodextrins for the preparation of complexes with pharmaceutical actives for use in controlled release products. See col 7 and examples. The reference exemplifies the use of pervaleryl- β -cyclodextrin.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare inclusion complexes of the prostaglandin, ONO-802, and pervaleryl-(α -, β -, or γ)-cyclodextrin to prepare a controlled release product. HIRAYAMA

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establishes that α -, β -, and γ -cyclodextrins form inclusion complexes with the prostaglandin, so in the absence of unexpected results, one of ordinary skill would expect success in preparing said complexes. An inclusion complex with pervaleryl- β -cyclodextrin would comprise 13.5 wt% of the guest prostaglandin.

Claims 19 and 86 are rejected under 35 U.S.C. 103(a) as being unpatentable over HIRAYAMA et al (Kobunshi Ronbunshi, 1982) and UEKAMA et al (US 5,904,929) as applied to claims 16-18 and 20-23 above, and further in view of HIRAYAMA et al (Chem. Pharm. Bull., 1995).

The invention is as set forth above. Claim 19 requires an acyl group having 1-4 carbon atoms. Claim 86 is drawn to an inclusion complex comprising triacetyl- α -cyclodextrin and a prostaglandin.

HIRAYAMA '82 teaches as set forth above.

UEKAMA teach as set forth above. The reference does not exemplify the use of acylated cyclodextrins having 1-4 carbon atoms, but specifically suggests the use of per- C_{2-18} acylated cyclodextrins.

HIRAYAMA '95 teaches that the rate of drug release from peracylated cyclodextrins is inversely proportional to the chain length of the acyl group. See abstract.

It would have been obvious to one having ordinary skill in the art to prepare inclusion complexes of the prostaglandin, ONO-802, and peracylated cyclodextrin for use in a controlled

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release product. It would be within the scope of the artisan to select the appropriate acyl for the desired activity. For a product having faster release, the artisan would select a shorter chain acyl, such as C_{1-4} . It would be further obvious to prepare a complex comprising triacetyl- α -cyclodextrin and the prostaglandin. The artisan would be motivated to select the simplest of these cyclodextrins to prepare a product having quicker release properties.

Claim 89 is rejected under 35 U.S.C. 103(a) as being unpatentable over UEKAMA et al (Int. J. Pharm., 1985) in view of HIRAYAMA et al (Chem. Pharm. Bull., 1995).

The invention is drawn to an inclusion complex comprising triacetyl- β -cyclodextrin and isosorbide-5-mononitrate.

UEKAMA teaches a complex comprising β -cyclodextrin and isosorbide-5-mononitrate (ISMN). The reference further teaches that ISMN pharmacologically equivalent to isosorbide dinitrate (ISDN) but is more useful than ISDN due to smaller individual blood levels. ISMN is stabilized by complexing with β -cyclodextrin. See page 339-340. The reference does not teach a complex comprising triacetyl- β -cyclodextrin.

HIRAYAMA teaches an inclusion complex comprising triacetyl- β -cyclodextrin and ISDN with utility for sustained release of the ISDN.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare an inclusion complex comprising triacetyl- β -cyclodextrin and ISMN. The practitioner would be motivated to prepare this in order to have an ISMN product

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stabilized by complexing with the cyclodextrin with the further utility of being a controlled release form.

Claim 90 is rejected under 35 U.S.C. 103(a) as being unpatentable over UMEMURA et al (Drug Design Deliv., 1990) in view of HIRAYAMA et al (Chem. Pharm. Bull., 1995).

The invention is drawn to an inclusion complex comprising triacetyl- β -cyclodextrin and nitroglycerin.

UMEMURA teaches an inclusion complex of nitroglycerin and diethyl- β -cyclodextrin having utility for preparing controlled release products. See page 297. The reference teaches that hydrophobic cyclodextrins are preferable to hydrophilic ones for controlling the release rate of the guest molecule.

HIRAYAMA '95 teaches as set forth above.

It would have been obvious to one having ordinary skill in the art to prepare an inclusion complex comprising nitroglycerin and triacetyl- β -cyclodextrin for preparing a controlled release product. In the absence of unexpected results, it would be within the skill of the artisan to select any of the peracetylated- β -cyclodextrins taught by HIRAYAMA '95 having this utility. The peracetylated species would be useful for a product in which a shorter release time was desired.

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Allowable Subject Matter

Claim 88 is allowed. UEKAMA '85 and HIRAYAMA '95 teach as set forth above. The art of record does not teach or fairly suggest the preparation of an inclusion complex comprising triacetyl-*alpha*-cyclodextrin and isosorbide-5-mononitrate. The fact that a compound, or one closely related, forms a complex with β -cyclodextrin does not make it obvious that the compound would form a complex with a similar α -cyclodextrin.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (703) 308-4525. The examiner can normally be reached on Monday-Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (703) 308-4624, may be contacted. The fax phone number for Group 1600, Art Unit 1623 is (703) 308-4556 or 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-1235.

Visit the U.S. PTO's site on the World Wide Web at <http://www.uspto.gov>. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more.



Leigh C. Maier
Patent Examiner
May 16, 2003